REMARKS

Claims 1-31 are now pending in the application. Claims 11, 16-19, and 27-28 have been withdrawn from consideration. Claims 1-10, 12-15, 20-26, and 29-31 have been rejected. Reconsideration and withdrawal of the rejections set forth in the Office Action dated April 15, 2004 are respectfully requested. Applicants petition the Commissioner for a 3-month extension of time: a separate petition accompanies this amendment.

I. Amendments

Claim 32 stands canceled.

Claim 1 is amended to more clearly define the invention. Basis for these amendments can be found on page 8, line 12 through page 12, line 4.

Claims 2, 8, 25, and 26 are amended to standardize terminology.

No new matter is added by way of these amendments.

II. Restriction Requirement

Claim 32 stands canceled. Applicants submit they have made a complete reply to the Restriction Requirement mailed March 25, 2003. Applicants reserve the right to pursue the subject matter of canceled claim 32 in a separately filed divisional application.

III. Rejections under 35 U.S.C. §103

Claims 1-10, 12-15, 20-24, 26 and 29-31 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Beumer, *et al.* (2003/0008397), optionally considering Valentini (U.S. Patent No. 6,428,579) or Clapper (U.S. Patent No. 5,744,515) for claim 15, and further in view of Maruyama, *et al.*, (U.S. Patent No. 5,597,456) or Li, *et al.*, (U.S. Patent No. 6,214,249).

Claims 1-9, 21-26, and 29-31 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Ikada, *et al.* (U.S. Patent No. 4,743,258), and further in view of Krause, *et al.* (U.S. Patent No. 5,500,257) or Ikada, *et al.* (JP 59-152913).

A. The Invention

The present invention describes a method of forming a coating having a selected surface density of a selected chemical group on the surface of a substrate. The method comprises the steps of:

(a) exposing the surface of the substrate to a plasma within a plasma chamber maintained substantially at atmospheric pressure, to form one or more active species on said substrate surface, until a desired surface density of the active species is formed;

(b) in the absence of exposure to plasma, exposing the surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group; and

(c) optionally contacting the exposed surface to a surface-modifying group under conditions effective to covalently attach the surface-modifying group to said functional group,

where the selected chemical group on the surface is the stable functional group or the surface-modifying group covalently attached thereto.

B. The Prior Art

BEUMER ET AL. disclose a process for coupling an adhesive glycoprotein to a surface of a material by depositing a volatile aldehyde from a gas plasma atmosphere on the surface of the material and then coupling the glycoprotein to the aldehyde layer. In the Beumer et al. approach, the volatile aldehyde deposited from a gas plasma atmosphere forms the stable functional groups to which the glycoprotein is attached. Nowhere does Beumer *et al.* show or suggest first forming active species on the surface of a substrate, then, in the absence of exposure to plasma, exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group.

VALENTINI discloses implantable prosthetic devices having a gold layer on the surface to which bioactive molecules are attached. The device is coated with gold by evaporation, electroplating, sputtering, or electrodeposition. The bioactive molecule is then attached to the gold using "simple chemistry techniques." Molecule coated polymer surfaces (FEP) were also prepared as a control. In this method, surface hydroxyl groups were added to cleaned FEP films by RF glow discharge under pressure. The peptides were rinsed and a peptide was then coupled to the hydroxyl groups. That is, the hydroxyl groups produced by glow discharge form the stable function groups to which the peptides are attached. Nowhere does this reference show or suggest first forming active species on the surface of a substrate, then, in the absence of exposure to plasma, exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group.

CLAPPER discloses a porous material having a surface chemistry that promotes capillary endothelialization. The material has a porosity that is sufficient to allow capillary endotheliazation. Clapper further discloses binding a cell adhesion molecule to promote ingrowth of endothelial cells into the pores of the material.

Nowhere does Clapper show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective, and in the absence of exposure to plasma, to convert an active species formed during plasma treatment to a stable functional group.

MARUYAMA ET AL. disclose a method of treating medical materials using atmospheric pressure glow discharge plasma. At least one surface of the material is exposed to a gas mixture comprising a glow-discharge-stabilizing gas and a treating gas, and subsequently applying an alternating current voltage to perform a plasma glow discharge treatment. Nowhere does Maruyama *et al.* show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective, and in the absence of exposure to plasma, to convert an active species formed during plasma treatment, to a stable functional group,.

LI ET AL. disclose a method of producing stable atmospheric pressure glow discharge plasmas using RF excitation. In the method, atmospheric pressure ionized gas mixtures are used to etch the organic material from a localized area of an organic substrate. Nowhere does Li *et al.* show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group in the absence of exposure to plasma.

IKADA ET AL. (THE '258 PATENT) disclose a blood-compatible material that includes a polymeric base material and water-soluble and substantially nonionic polymers directly attached to the surface of the base material. The polymers may be attached by forming radicals or peroxides on the surface of the base material and contacting the monomer(s) with the base. The radicals or peroxides may be formed by i.e. low-temperature plasma discharge. Nowhere does the '258 patent show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group.

KRAUSE ET AL. describe a method of preparing a fluoropolymer composite tube for use in gas lines. The tube is prepared by activating a formed fluoropolymer substrate by subjecting the substrate to a charged gaseous atmosphere formed by electrically ionizing a gas and subsequently applying a layer of a thermoplastic polymer to the activated fluoropolymer. The ionizing step may be a corona discharge or electrically formed plasma. Nowhere does Krause *et al.* show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group, in the absence of exposure to plasma.

IKADA ET AL. (THE '913 PUBLICATION) disclose a method of modifying the surface of a polymeric material by treating the surface of the polymeric material with corona discharge in open atmosphere and carrying out the graft polymerization of a radically polymerizable monomer to the surface. Nowhere does the '913 publication show or suggest exposing a substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group.

C. Analysis

According to the MPEP § 2143, one of the three basic criteria to establish a *prima facie* case of obviousness is that the prior art references (or references when combined) must teach or suggest all the claim limitations.

1. Rejection over Beumer *et al.*, optionally considering Valentini or Clapper, and further in view of Maruyama *et al.* or Li *et al.*

The present invention, as amended, claims a method of forming a coating on the surface of a substrate. The method includes a step of exposing the surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of

exposure to plasma. As noted above, none of the references show or suggest this claimed step.

Beumer *et al.* disclose forming volatile aldehyde groups on the substrate surface. These groups are then reacted with the amino groups of the glycoprotein to bind the glycoprotein to the substrate surface. Nowhere do Beumer *et al.* disclose stabilizing the volatile aldehyde groups. Nor would one modify Beumer *et al.* to stabilize the reactive groups as they are essential to bind the monomer(s), which is the goal of Beumer *et al.*

Nor does the teaching in any of Valentini, Clapper, Maruyama *et al.*, or Li *et al.* make up for this deficiency in Beumer *et al.* While Maruyama *et al.* disclose exposing the surface material to a glow discharge-stabilizing gas, the stabilizing gas is mixed with the treatment gas and exposed to the surface under plasma conditions. Thus, Maruyama *et al.* cannot be said to teach exposing the surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of exposure to plasma. Li *et al.* does not even teach exposing the surface of the substrate to plasma to form one or more active species, much less further exposing the surface to a selected gas or liquid to convert the active species to a stable functional group.

The Valentini and Clapper references are cited merely for a teaching of the cell-adhesion molecule disclosed in claim 15. Neither Valentini nor Clapper make up for the shortcoming in the combination of Beumer *et al.* in view of Maruyama *et al.* or Li *et al.*, as discussed above, as neither reference makes any mention of exposing the substrate surface to a selected gas or liquid to convert the active species to a stable functional group.

Accordingly, none of the references, alone or in combination, show or suggest exposing the substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group in the absence of exposure to plasma. Accordingly, Applicants respectfully request withdrawal of the rejections under 37 C.F.R. § 103.

2. Rejection over the '258 patent in view of Krause *et al.* or the '913 publication

As discussed above, the method of the invention includes a step of exposing the substrate surface to a selected gas or liquid under conditions effective to convert the active species (formed by plasma deposition) to a stable functional group in the absence of exposure to plasma. Each of the cited '258 patent, Krause *et al.*, and '913 publication fail to show or suggest this step.

In the method described in the '258 patent, highly reactive radicals or peroxides are formed on a base material. The base material is then exposed to monomer(s) to attach the monomer(s) to the base material. Nowhere does the '258 patent disclose stabilizing the reactive radicals or peroxides. Nor would one modify the '258 patent to stabilize the reactive groups as the groups are essential to bind the monomer(s), which is the ultimate goal of the '258 patent.

Neither Krause *et al.* nor the '913 application make up for this deficiency in the '258 patent. Krause *et al.* teach activating a fluoropolymer substrate by subjecting the substrate to a charged gaseous atmosphere. A layer of a thermoplastic polymer is then applied to the activated fluoropolymer. Nowhere does Krause *et al.* disclose stabilizing the active groups formed on the substrate. Nor would one stabilize these groups as they bind to the thermoplastic layer, a necessary feature of Krause *et al.*

The '913 publication also fails to show or suggest exposing the surface of the substrate to a plasma to form one or more active species and then converting the active species to a stable functional group. In the method of the '913 publication, the surface of a polymeric material is treated with corona discharge and then graft polymerization of a radically polymerizable monomer to the surface is carried out.

Accordingly, none of the references, alone or in combination, show or suggest exposing the substrate surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group. Accordingly, Applicants respectfully request withdrawal of the rejections under 37 C.F.R. § 103.

IV. Obvious-Type Double Patenting Rejections

Claims 1-10, 12-15, 20-24, 26, and 29-31 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-9 and 11-16 of U.S. Patent No. 6,159,531 in view of Beumer *et al.* (2003/0008397), and further in view of Maruyama *et al.* ('456) or Li *et al.* ('249).

Claims 1-10, 21-26, and 29-31 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-9 and 11-16 of U.S. Patent No. 6,159,531 in view of Ikada *et al.* ('258), and further in view of Krause *et al.* ('257) or Ikada *et al.* ('913).

Applicants respectfully traverse these rejections.

A. The Present Invention

As noted above, the present invention includes the steps of:

(a) exposing the surface of the substrate to a plasma within a plasma chamber maintained substantially at atmospheric pressure, to form one or more active species on said substrate surface, until a desired surface density of the active species is formed;

(b) in the absence of exposure to plasma, exposing the surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group; and

(c) optionally contacting the exposed surface to a surface-modifying group under conditions effective to covalently attach the surface-modifying group to said functional group,

where the selected chemical group on the surface is the stable functional group or the surface-modifying group covalently attached thereto.

B. The 6,159,531 Patent

The claims in Patent No. 6,159,531 relate to a method of treating a medical device briefly comprising:

plasma cleaning the device surface exposed to tissue and/or blood;

functionalizing the surface to provide a plasma-deposited layer having functional groups; and

subjecting the plasma-deposited layer to multifunctional linkers/spacers to form covalent bonds between the linkers/spacers and the functional groups.

C. Analysis

The method of the present invention includes a step of exposing the surface to a selected gas or liquid under conditions effective to convert the active species to a stable functional group in the absence of exposure to plasma.

While the method of the '531 patent provides a plasma-deposited layer having functional groups and subjects the layer to multifunctional linkers/spacers to form covalent bonds between the linkers/spacers and the functional groups (optional in the present invention), the '531 patent makes no mention of an intermediate step of converting the active species to a stable functional group, much less converting the active species in the absence of exposure of plasma.

Nor do the cited Beumer *et al.*, Maruyama *et al.*, Li *et al.*, Ikada *et al.* ('258), Krause *et al.*, or Ikada *et al.* ('913) references make up for this lack of teaching for the reasons given above in section III.

In view of the above, Applicants submit that the invention as presently claimed is patentably distinct from U.S. Patent No. 6,159,531. Accordingly, Applicants respectfully request withdrawal of the rejection under the judicially created doctrine of obviousness-type double patenting.

V. Conclusion

In view of the foregoing, Applicants submit that the claims pending are in condition for allowance. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,

Date: Oct. 15, 2004

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